Vision Research 93 (2013) 49–53

Contents lists available at ScienceDirect

Vision Research

journal homepage: www.elsevier.com/locate/visres

Patients with schizophrenia show deficits on spatial frequency doubling

Neda Khosravani, Mohammad Ali Goodarzi *

Department of Clinical Psychology, College of Education and Psychology, Shiraz University, Shiraz, Iran

ARTICLE INFO

Article history:
Received 27 July 2012
Received in revised form 4 October 2013
Available online 16 October 2013

Keywords:
Attention
Magnocellular
Humphrey perimetry test
Spatial frequency
Visual sensitivity

ABSTRACT

There are pieces of evidence indicating that visual deficits in patients with schizophrenia can be attributed to a deficiency in the magnocellular portion of the early visual system. The main objective of this study was to investigate the neurological dysfunction of the magnocellular pathway in patients with schizophrenia using the frequency doubling technology perimetry (FDT). The FDT has been developed based on particular neural magnocellular characteristics and can examine the magnocellular dysfunction hypothesis in schizophrenia. Twenty patients with schizophrenia (12 males and 8 females) and 20 normal subjects (10 males and 10 females) participated in this study. The spatial frequency doubling task was presented via the Humphrey perimetry instrument in order to examine the magnocellular pathway of the participants. Patients with schizophrenia showed less visual field sensitivity than normal controls and their standardized age cohort in both eyes ($p < 0.001$). The results indicated impaired visual field sensitivity deficits in patients with schizophrenia that can be attributed to a deficit in the magnocellular neural pathways. This Magnocellular pathway defect may provide a physiological base to explain some of the deficits caused by schizophrenia such as cognitive deficits.

1. Introduction

Visual processing deficits in schizophrenia have long been considered by researchers. Earlier research had shown that patients with schizophrenia have deficits in visual integration and normal backward masking (Saccuzzo & Braff, 1981). More recent research indicated reduced contrast sensitivity (Butler & Javitt, 2005), reduced visual ERP amplitudes (ERPs), increased thresholds for evaluation of visual stimuli (Butler et al., 2005; Slaghuis, 1998), reduced neurophysiologic response to a single stimulus (Butler et al., 2001), deficits in motion processing (e.g. Chen et al., 2004), and deficits in spatial–temporal integration (Makarem et al., 2010) in patients with schizophrenia. The relation between these deficits is not well understood.

Some researchers have proposed that a portion of these visual processing deficits might be attributed to a potential malfunction of the magnocellular pathway in patients with schizophrenia (e.g., Kim et al., 2006; Martinez et al., 2008; Schechter et al., 2003).

The visual pathway consists of three main streams: Magnocellular, Parvocellular, and Koniocellular. The Magnocellular stream (M cells) is responsible for transferring low spatial frequency and high temporal frequency information, i.e. it is responsible for vision in low light and seeing moving objects. The Parvocellular pathway (P cells) is responsible for transferring high spatial frequency and low temporal frequency information, i.e. it is responsible for detailed vision and seeing static objects. The Koniocellular pathway (K cells) is responsible for transferring short or blue wavelength (Mashayekhy et al., 2008). It is expected that magnocellular deficits emerge at low spatial frequencies (e.g. 1.5 c/deg) and high temporal frequencies (Skottun & Skoyles, 2007a).

Research have shown that the magnocellular pathway transfers information related to movement, stereopsis, spatial localization, depth perception, hyperacuity, figural grouping, illusory border perception, and figure/ground separation (Livingstone, 1987; as cited in Patel, 2004).

A magnocellular pathway dysfunction has been reported by several investigators in patients with schizophrenia using different techniques. Martinez et al. (2008) reported a reduced activity to low spatial frequencies (but not high spatial frequencies) in several areas of the parietal and temporal lobes using functional magnetic resonance imaging. Kim et al. (2006) showed that deficits in motion processing in schizophrenia are significantly associated with reduced activity of the magnocellular vision systems using steady state Visual Evoked Potentials (ssVEP). Schechter et al. (2003) showed a significant functional impairment in schizophrenic patients' magnocellular pathways using a backward masking task. It has also been observed that patients with schizophrenia have reduced electrophysiological activity for magnocellular oriented stimuli (Butler et al., 2001).

Another effective and reliable way to separate magnocellular activities in psychosomatic tests is the measurement of contrast sensitivity (Skottun & Skoyles, 2007a). Studies on injuries to different layers of Lateral Geniculate Nucleus (LGN) of monkeys found

* Corresponding author. Fax: +98 711 6134651.
E-mail address: mgoodarzi@rose.shirazu.ac.ir (M.A. Goodarzi).

0042-6989/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.visres.2013.10.007

that reduction in contrast sensitivity following injury in magnocellular layers is limited to cases where stimuli are of low spatial frequency or high temporal frequency (Merigan, Byrne, & Maunsell, 1991a; Merigan, Katz, & Maunsell, 1991b; Merigan & Maunsell, 1990, 1993; Schiller, Logothetis, & Charles, 1990a, 1990b; as cited in Skottun & Skoyles, 2007a). Psychosomatic studies on humans are consistent with these findings (Legge, 1978, Tolhurst, 1975; as cited in Skottun & Skoyles, 2007a).

Several studies have reported significant differences between patients with schizophrenia and the control groups in different spatial contrast sensitivity tasks indicative of magnocellular inefficiency (e.g., Butler et al., 2005; Keri et al., 2002; O'Donnel et al., 2006; Revheim et al., 2006; Schwartz, McGinn, & Winstead, 1987; Slaghuis, 1998, 2004; Slaghuis & Bishop, 2001; Slaghuis & Thompson, 2003).

Some studies investigated spatial and temporal frequencies via a combined method. In a study by Keri et al. (2005), a spatial origin task was used. The results of this study showed that, like their biological relatives, patients with schizophrenia – under both medication and non-medication – have more definitive deficits in situations of low contrast and doubled frequency compared to consistent lighting. These findings support the magnocellular deficits in schizophrenia, because low contrast and doubled frequency are likely indicators of magnocellular inefficiency. Chen et al. (2004) showed varying degrees of reduced sensitivity for part of subjects with schizophrenia. In contrast, Keri et al. (2000), Gutherie, McDowell, and Hammond (2006) and Delord et al. (2006), found no deficits related to magnocellular malfunction in patients with schizophrenia.

Research conducted to date has investigated the magnocellular deficits in schizophrenia and other disorders using different tasks. Each of these tasks considers a specific deficit in schizophrenia (e.g. backward masking, motion processing, contrast sensitivity, etc.) or measures low spatial frequencies or high temporal frequencies which are features of the magnocellular pathway. There are many disputes about the reliability and validity of these instruments. Although the results of these studies, are consistent with the magnocellular system malfunction in schizophrenia disorder, some other studies tend to disprove them (e.g. Barch et al., 2003; Braus et al., 2002; Delord et al., 2006; Gutherie, McDowell, & Hammond, 2006; Selemon & Begovic, 2007; Skottun & Skoyles, 2007a, 2007b; Slaghuis & Bishop, 2001). There are substantial controversies over research methods and it seems that a measurement instrument is required that specifically focuses on features unique to the magnocellular pathway and which evaluates its function validly and reliably.

Kelly (1966; as cited in Patel, 2004) introduced a phenomenon named the doubled frequency illusion. In this frequency-doubling task the stimuli include alternating black and white stripes with low spatial frequency (0.25 c/deg). The place of these white and black stripes changes alternatively with high temporal frequency (25 Hz) creating a flickering appearance. In this situation, the number of black and white stripes appears to be doubled.

In the 1990s, this phenomenon was linked to a subset of type M (Magnocellular) cells that could selectively become damaged in glaucoma. Since then many researchers have studied this phenomenon (Maddess & Henry, 1992; Quigley et al., 1987; Johnson, 1994; Johnson & Samuel, 1997; Maddess et al., 1999; Maddess & Severt, 1999; Kalaboukhova & Lindblom, 2003, all cited in Patel, 2004). It is believed that the perception of this low spatial frequency sinusoidal grating with high flickering temporal frequency occurs due to the non-linear magnocellular mechanisms (Johnson & Demirel, 1997).

The Humphrey Matrix is the latest perimetry generation of frequency doubling technology (FDT) which was developed in 2003 with seven functional tests for the eye care professions (Patel, 2004). It is considered as a detailed, fully equipped and reliable visual field testing instrument that evaluates the magnocellular pathway directly taking into account its special features. Doubled frequency perimetry provides a contrast sensitivity test for detecting magnocellular pathway deficit (Anderson & Johnson, 2003). Many studies have shown that doubled frequency perimetry can detect impairments in the visual field that are overlooked by other methods (Dublin, 2003). The Humphrey Matrix has high differential ability in detecting early functional damage in patients at risk (Spry et al., 2005; as cited in Zeppieri & Johnson, 2008). Various studies have provided promising results using the Humphrey Matrix which is the result of its precision, accuracy, sensitivity, specificity, and reliability (Johnson et al., 1999; Turpine et al., 2003; Arts et al., 2005; Anderson & Johnson, 2005; all cited in Zeppieri & Johnson, 2008).

The FDT visual field instrument selectively examines the magnocellular visual pathway (Patel, 2004), but has not previously been used to investigate visual function in schizophrenia. This study utilizes doubling frequency technology to test the magnocellular deficit hypothesis in patients with schizophrenia.

2. Materials and methods

2.1. Design

The research method for this study was causal–comparative. The independent variable was schizophrenia (belonging to the group) and the dependent variable was Magnocellular deficit measured through evaluation of visual field sensitivity by means of Humphrey perimetry frequency doubling technology.

2.2. Subjects

The experimental group included all non-hospitalized patients with schizophrenia who referred to Hafez Hospital, Shiraz. The control group included eye clinic staff and patients' companions. The sample included 20 patients (12 males and 8 females) and 20 healthy persons (10 males and 10 females) as control group. Inclusion criteria for the experimental group (selected via convenience sampling method) restricted to patients in the 18–50 years old age range, with normal vision (20/20 as tested by Snellen chart), and with a diagnosis of acute schizophrenia, as diagnosed by a psychiatrist based on clinical interview. The patients were selected based on DSM-IV-TR diagnostic criteria. The exclusion criteria included physical and mental illnesses apart from the main diagnosis (such as drug abuse, mental retardation or having a severe emotional disturbance). The control group participants were selected via convenience sampling method. The exclusion criteria for this group included any psychiatric diagnosis or history of psychiatric diagnosis, neurological illness, head injury, accident or medical eye disorders. A review of these variables was accompanied by participants' or their companions' reports.

Patients, who referred to Department of Psychiatry in Hafez Hospital and had schizophrenia diagnosis, were referred to the researcher by the psychiatrist. After interviewing each patient and ensuring that they met the criteria of schizophrenia and other inclusion criteria, the researcher explained the perimetry test and its duration and the purpose of research. The patients were told that the test was performed in the eye ward of Shiraz Motahari Clinic. The patients who agreed with all of these conditions signed "the informed consent form to participate in research project" that included the name of the research project, and the related school and executives, confidentiality issues, benefits, the right to reject or cancel, and response to all questions. Any expenses including patients' travelling and testing costs were incurred by the researcher. Both of the patient's eyes were tested using the

Humphrey Matrix perimetry test in the 24–2 mode, in the test room by trained personnel. All patients were on different doses of antipsychotic medication.

2.3. Materials and stimuli

2.3.1. Frequency doubling Humphrey Matrix

The Humphrey Matrix is the latest generation of perimetry frequency doubling technology. It (30 cm × 56 cm × 43 cm, 14 kg) includes a liquid crystal menu display screen, a video eye monitor, a patient visor, and a patient response button as well as separate full keyboard with a track pad and an external printer and internal software. The Humphrey Matrix has many advantages, such as ease of application and interpretation of results. Moreover, it is not affected by cataract and refractive errors (large stimuli eliminate the need for trial lens correction) and it has rapid test methods (less than 5 min per eye). The test has high test–retest reliability (Zeppieri & Johnson, 2008). Another important advantage is that the test can be scheduled and automated to prevent any possible changes on the part of the examiner (Riordan-Eva, Vaughan, & Asbury, 2003).

2.3.2. Stimulus

The 24–2 test that was used in this study is one of the seven tests of the Humphrey Matrix which uses 5° square stimuli that are presented at random order with counter-phase flickering method with temporal frequency of 18 Hz and spatial frequency of 0.5 c/deg and tests 55 locations. Quantitative measurements of the visual field in each location of Humphrey Matrix tests are compared to a database normalized with more than 270 people (18–85 years). In fact, in this type of test, doubled frequency sinusoidal stimuli which included black and white stripes quickly replacing each other in a small square, are shown for 300 ms (per stimulus) in different parts of the visual field. The mean test background illumination was set at 100 cd/m. Contrast ranges varied from 38 dB to 0 dB. The subject was supposed to rest his or her forehead on the visor without the assistance of a chin rest and every time saw one of the stimulus, push a button that was located in his or her hand so that the system would record his/her answers.

2.3.3. Researcher-made questionnaire

The other research instrument was a self-report questionnaire developed by the researcher which measured age, sex, and other variables such as time since which treatment has begun and lifetime history of any physical or mental illnesses.

3. Results

Among 20 cases of schizophrenic patients in this study, one patient had no history of hospitalization. Other patients had between 1 and 6 incidences of psychiatric hospitalization. Two patients had no history of receiving ECT and others received ECT 1–22 times. Three of these patients were of type II and type I schizophrenia and the rest had been receiving treatment since 8 months to 21 years before. At the time of study none were hospitalized, but all were taking antipsychotic medications. The average number of hospitalizations for patients in general was 7 times and the average amount of time patients were under psychiatrists' supervisions was 82 months. Demographic characteristics of groups have been presented in Table 1.

Although, the two groups were not equal in terms of gender due to the low number of female patients with schizophrenia, Fisher exact test showed that the two groups were not statistically different in terms of gender. This coefficient was equal to 0.75 (df = 1, $p > 0.05$). Independent samples t-test indicated that the groups did not differ significantly in terms of education ($t = 1.159$, df = 38, $p > 0.05$) and age ($t = 0.90$, df = 38, $p > 0.05$).

Table 1
Demographic characteristics (age and gender) of groups.

Groups	n	Man	Woman	Age range	Mean	SD
Schizophrenia	20	12	8	19–45	28.25	7.77
Normal's	20	10	10	20–40	30.25	6.18

FDT provides a mean deviation (MD) index to generally summarize the visual field results for threshold tests. MD represents the average sensitivity deviation from a normal healthy person of the same age (based on the normative data base). The MD is an indication of the overall visual field sensitivity, and can either be a negative or positive value depending on if the individual's general contrast sensitivity is below or above the average for that same age group. A defective visual field is presented by a negative value. MD is relatively insensitive to localized defects and is strongly affected by generalized trends and thus negative MDs are an indication of abnormal magnocellular visual pathway (Zeppieri & Johnson, 2008). Table 2 shows the mean and standard deviation of MD scores for groups in left and right eyes.

In order to examine whether patients with schizophrenia and normal controls demonstrated different visual field sensitivity in the right and left eyes, the mean deviation scores were subjected to a 2 × 2 repeated measures ANOVAS with group (schizophrenia and normals) as between subject factor and the eyes (left and right) as within subject factor. The main effects were significant: group [df = (38, 1), $F = 50.1$, $p < 0.001$], eyes [df = (38, 1), $F = 4.89$, $p < 0.03$]. However, the group × eyes interaction was not significant [df = (38, 1), $F = 3.45$, $p < 0.07$]. Overall, the results show that patients with schizophrenia have less visual field sensitivity than normal controls in both eyes. In addition, irrespective of group, total visual field sensitivity is less in the right eye ($M = -1.92$, SE = .57) than the left eye ($M = -3.31$, SE = .73). Independent t-tests for each eye showed a significant difference between the two groups in both eyes (see Table 3).

FDT provides three reliability indices to verify whether or not test results are valid. The reliability indices check for fixation errors in addition to false negative and false positive errors. If one of these values had gone out of 20%, the system was stopped and the experimenter repeated the test. Table 4 shows these indices (the ratio of errors) for patients with schizophrenia and normal controls in left and right eyes. These data shows that the averages of errors are about .05% or 5%.

Table 2
Mean and SDs of visual field sensitivity for both eyes by groups.

Subjects	Right eye	Left eye
Schizophrenia ($n = 20$)	−8.15 (6.21)	−5.06 (4.87)
Normal's ($n = 20$)	1.32 (1.56)	1.54 (1.68)

Table 3
Results of independent t-tests for each eye for the two groups of subjects.

Eye location	Levene's test for equality of variances		t-test for equality of means			
	F	Significant	t	df	Mean difference	Sig. (2-tailed)
Right	26.55	0.001	6.615	21.407	9.47	0.001
Left	10.78	0.002	5.729	23.481	6.61	0.001

Table 4
Mean and SDs of the ratio of errors for both eyes in groups.

Subjects	Errors	Right eye		Left eye	
		M	SD	*M*	SD
Schizophrenia ($n = 20$)	Fixation	.09	0.13	.06	.09
	False positive	.03	.05	.02	.05
	False negative	.08	.08	.06	.10
Normals ($n = 20$)	Fixation	.03	.05	.05	.06
	False positive	.04	.05	.05	.07
	False negative	.04	.09	.05	.08

Table 5
Repeated measures ANOVA for Group × Errors × Eyes.

	Source of variance		
	df	*f*	*p*
Group	1,38	1.24	.27
Eyes	1,38	.15	.70
Group × Eyes	1,38	3.34	.08
Errors	1,38	.09	.76
Group × Errors	1,38	.16	.69
Errors × Eyes	1,38	.03	.87
Group × Errors × Eyes	1,38	.20	.66

Groups: patients with schizophrenia and normal's; eyes: left and right; errors: fixation errors, false positive errors and false positive errors.

The ratio of errors were subjected to a 2 × 2 × 3 repeated measures ANOVAS with group (schizophrenia and normals) as between subject factor and eyes (left and right) and errors (fixation errors, false positive errors and false negative errors) as within subject factors. None of the main effects and interactions was significant (Table 5). This indicates that the errors were not significantly different in both groups and both eyes.

4. Discussion

This study was designed to examine the extent of magno-defict involvement in schizophrenia using the frequency doubling technology. Frequency doubling technology has been used in several studies not related to schizophrenia to determine magnocellular pathway deficiencies (Patel, 2004). The results from current study provide support for a magno deficit in schizophrenia. Patients with schizophrenia showed less sensitivity to the frequency doubling stimuli compared to the normal group as well as a significant decrease in sensitivity compared to their standardized age cohort (except for one patient, the rest of patients showed a negative score in Humphrey's test, indicative of a deficit in magnocellular pathway). This deviation was not apparent with the normal group who demonstrated sensitivity comparable to their age group.

This result is consistent with the findings of several other studies which used contrast sensitivity to detect magnocellular deficiency in patients with schizophrenia (see Skottun & Skoyles, 2007a for a review). As mentioned earlier, the effect of doubled frequency created by a low spatial frequency combined with a high temporal frequency is essential for preferential stimulation of magnocellular cells with a good technique. In fact, the values of contrast sensitivity for doubled frequency stimuli are more effective in detecting magnocellular deficits than when each spatial or temporal frequency is presented separately (Johnson & Demirel, 1997).

The result of the current study is consistent with the results of several other studies indicative of abnormality in low-level sensory processing (e.g. Butler et al., 2005; Slaghuis, 2004), motion tracking, trajectory and spatial localization (O'Donnel et al., 1996 as cited in Martinez et al., 2008; Chen et al., 1999, 2003, 2004; Lee, 2002; Brenner et al., 2003; Keri et al., 2004; Steve et al., 1997; all cited in Butler et al., 2005), electrophysiological recordings of ERPs (Butler et al., 2007; Schechter et al., 2005), electrophysiological activity of Magnocellular oriented stimuli (Butler et al., 2001; as cited in Schechter et al., 2003), visual integration, and backward masking (Saccuzzo & Braff, 1981) in patients with schizophrenia.

The result of this study is also consistent with the results of several other studies on spatial frequency (Keri et al., 2002; Slaghuis, 1998, 2004; Slaghuis & Thompson, 2003), temporal frequency (Chen et al., 2003; Laycock, Crewther, & Crewther, 2007; O'Donnel et al., 2006; Schwartz, McGinn, & Winstead, 1987; Slaghuis & Bishop, 2001), and combining both temporal and spatial frequencies (Chen et al., 2004; Cimmer et al., 2006; Delord et al., 2006; Gutherie, McDowell, & Hammond, 2006; Keri, 2008; Keri et al., 2005) in patients with schizophrenia.

Skottun and Skoyles (2007a) in a research review on contrast sensitivity and magnocellular functioning in schizophrenia came to the conclusion that the studies on contrast sensitivity in patients with schizophrenia provide little evidence for a magnocellular deficit. They attributed contrast sensitivity reductions in patients with schizophrenia to attentional problems. They also declared that attention deficit is probably unrelated to vision; as such problems can arise out of flawed performance of pre-frontal cortex (Skottun & Skoyles, 2007a). Although the result of this study cannot reject the above conclusion completely and attentional problems might exert some effect on the response of patients, the task checks for attentional distractions via monitoring fixations error, false positive and false negative errors. The analysis of reliability indices showed that the test results are valid when we consider fixation, false positive and false negative errors. In addition, the selective impairment of the magnocellular system in glaucoma and the ability of frequency doubling technology to illustrate these impairments have been previously well documented (Maddess et al., 1999).

Butler et al. (2001), Keri et al. (2002), and Butler et al. (2005) postulate that early stage visual processing deficits significantly predict higher level cognitive impairments. Martinez et al. (2008) showed that the sensory processing deficits can be related to high levels of cognitive impairment, active memory, executive function and attention. Therefore, it is possible that magnocellular deficits in patients with schizophrenia can affect higher cognitive systems.

Recent studies that suggest visual processing deficits in schizophrenia, especially in tasks such as motion tracking, trajectory and spatial localization (Chen et al., 1999, 2003; Lee, 2002; Brenner et al., 2003, Keri et al., 2004; Steve et al., 1997; O'Donnel et al., 1996, as cited in Butler et al., 2005) reflect dorsal visual pathway malfunction, because the dorsal pathway receives initial information from the Magnocellular pathway, Deficits in Magnocellular performance may also affect higher level malfunction of dorsal visual pathway.

Since all patients were taking antipsychotic medications, the results of this study are not able to exclude the effect of medications on the performance of patients with schizophrenia in frequency doubling test. Several previous studies on visual processing (Brody et al., 1980; Braff & Saccuzzo, 1982; Harvey et al., 1990; as cited in Martinez et al., 2008; Butler et al., 1996, 2003; Kadenhed et al., 1997; Harvey et al., 1990, as cited in Butler et al., 2005), contrast sensitivity (O'Donnel et al., 2006), motion-processing (Chen et al., 1999, as cited in Kim et al., 2006), and backward masking deficits in patients with schizophrenia were not related to antipsychotics. For example, Butler et al.'s study (1996, 2002; as cited in Schechter et al., 2003) and a study by Keri et al. (2005) showed that patients with schizophrenia (both with and without medication) invariably show deficits in low contrast situations and doubled frequency. Thus, while antipsychotics are an important issue, there is little evidence to support this notion. However, future studies should examine patients at early stages of schizophrenia or those who are genetically vulnerable to schizophrenia.

In general, the results from the current study provide good evidence for magno system involvement in schizophrenia. While we suspect that visual deficits may play a causal role in some of the deficits caused by the disease (i.e. cognitive deficits), we note that schizophrenic perceptual difficulties are clearly not limited to vision.

References

Anderson, A. J., & Johnson, C. A. (2003). Frequency-doubling technology perimetry. *Ophthalmology Clinical North American, 16*, 213–225.

Barch, D. M., Mathews, J. R., Buckner, R. L., Maccotta, L., Csernansky, J. G., & Snyder, A. Z. (2003). Hemodynamic responses in visual, motor, and somatosensory cortices in schizophrenia. *Neuroimage, 20*, 1884–1893.

Braus, D. F., Weber-Fahr, W., Tost, H., Ruf, M., & Henn, F. A. (2002). Sensory information processing in neuroleptic-naive first-episode schizophrenic patients: A functional magnetic resonance imaging study. *Archives of General Psychiatry, 59*, 696–701.

Butler, P. D., Desanti, L. A., Maddox, J., Harkavey-Friedman, J. M., Amador, X. F., Goetz, R. R., et al. (2003). Visual backward-masking deficits in schizophrenia: Relationship to visual pathway function and symptomatology. *Schizophrenia Research, 59*, 199–209.

Butler, P. D., & Javitt, D. C. (2005). Early-stage visual processing deficits in schizophrenia. *Current Opinion in Psychiatry, 18*, 151–157.

Butler, P. D., Martinez, A., Foxe, J. J., Kim, D., Zemon, V., Silipo, G., et al. (2007). Subcortical visual dysfunction in schizophrenia drives secondary cortical impairments. *Experimental Brain Research, 130*, 417–430.

Butler, P. D., Zemon, V., Schechter, I., Saperstein, A. M., Hoptman, M. J., Lim, K. O., et al. (2005). Early-stage visual processing and cortical amplification deficits in schizophrenia. *Archives of General Psychiatry, 62*, 495–504.

Butler, P. D., Zemon, V., Schechter, I., Zemon, V., Schwartz, S. G., Greenstein, V. C., et al. (2001). Dysfunction of early-stage visual processing in schizophrenia. *American Journal of Psychiatry, 158*, 1126–1133.

Chen, Y., Levy, D. L., Sheremata, S., & Holzman, P. S. (2004). Compromised late-stage motion processing in schizophrenia. *Biological Psychiatry, 55*, 834–841.

Chen, Y., Levy, D. L., Sheremata, S., Nakayama, K., Matthysse, S., & Holzman, P. S. (2003). Effect of typical, atypical and no antipsychotic drugs on visual contrast detection in schizophrenia. *American Journal of Psychiatry, 160*, 1795–1801.

Cimmer, C., Szendi, I., Csifcsak, G., Szekeres, G., Kovacs, Z. A., Somogyi, I., et al. (2006). Abnormal neurological signs, visual contrast sensitivity, and the deficit syndrome of schizophrenia. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 30*, 1225–1230.

Delord, S., Ducato, M. G., Pins, D., Devinck, F., Thomas, P., Boucart, M., et al. (2006). Psychophysical assessment of magno- and parvocellular function in schizophrenia. *Visual Neuroscience, 23*, 645–650.

Dublin, C. A. (2003). Humphrey matrix visual field instrument. User's guide. *Zeiss carl Zeiss meditec*, part no. 112738 Aev A.

Gutherie, A. H., McDowell, J. E., & Hammond, B. R. Jr., (2006). Scotopic sensitivity in schizophrenia. *Schizophrenia Research, 84*, 378–385.

Johnson, C. A., & Demirel, S. H. (1997). The role of spatial and temporal factors in frequency-doubling perimetry. *Perimetry update* (pp. 13–19).

Kelly, E. H. (1966). Frequency doubling in visual responses. *Journal of the Optical Society of America, 56*, 1628–1633.

Keri, S. (2008). The magnocellular pathway and schizophrenia, letter to the editor. *Vision Research, 48*, 1181–1182.

Keri, S., Antal, A., Szekeres, G., Benedek, G., & Janka, Z. (2000). Visual information processing in patients with schizophrenia: Evidence for the impairment of central mechanisms. *Neuroscience Letters, 293*, 69–71.

Keri, S., Antal, A., Szekeres, G., Benedek, G., & Janka, Z. (2002). Spatiotemporal visual processing in schizophrenia. *Journal of Neuropsychiatry and Clinical Neuroscience, 14*, 190–196.

Keri, S., Kelemen, O., Janka, Z., & Benedek, G. (2005). Visual perceptual dysfunction are possible endophenotypes of schizophrenia: Evidence from the psychophysical investigation of magnocellular and parvocellular pathways. *Neuropsychology, 19*, 649–656.

Kim, D., Wylie, G., Pasternak, R., Butler, P. D., & Javitt, D. C. (2006). Magnocellular contributions to impaired motion processing in schizophrenia. *Schizophrenia Research, 82*, 1–8.

Laycock, R., Crewther, S. G., & Crewther, D. P. (2007). A role for the 'magnocellular advantage' in visual impairments in neurodevelopmental and psychiatric disorders. *Neuroscience and Biobehavioral Reviews, 31*, 363–376.

Maddess, T., Goldberg, I., Dobinson, J., Wine, S., Welsh, A. H., & James, A. C. (1999). Testing for glaucoma with the spatial frequency doubling illusion. *Vision Research, 39*, 4258–4273.

Makarem, S., Goodarzi, M. A., Taghavi, M. R., & Rahimi, C. (2010). A comparison between performance of patients with schizophrenia, major depression and normal controls in spatio-temporal integration task. *Journal of Psychology, 54*, 114–130.

Martinez, A., Hillyard, S. A., Dias, E. C., Hagler, D. J., Jr., Butler, P. D., Guilfoyle, D. N., et al. (2008). Magnocellular pathway impairment in schizophrenia. Evidence from functional magnetic resonance imaging. *Journal of Neuroscience, 28*, 7492–7500.

Mashayekhy, G., Miranbeigi, M., Nilforushan, N., & Sepehr, R. (2008). Recent developments in automated perimetry. *Bina Journal of Ophthalmology, 13*(2), 244–258.

O'Donnel, B. F., Bismark, A., Hetrick, W. P., Bodkins, M., Vohs, J. L., & Shekhar, A. (2006). Early stage vision in schizophrenia and schizotypal personality disorder. *Schizophrenia Research, 86*, 89–98.

Patel, N. (2004). The use of frequency doubling technology to determine magnocellular pathway deficiencies. *Journal of Behavioral Optometry, 15*, 31–36.

Revheim, N., Butler, P. D., Schechter, I., Jalbrzikowski, M., Silipo, G., & Javitt, D. C. (2006). Reading impairment and visual processing deficits in schizophrenia. *Schizophrenia Research, 87*, 238–245.

Riordan-Eva, P., Vaughan, D., & Asbury, T. (2003). In P. Riordan-Eva & J. P. Whicher (Eds.), *Vaughan & Asbury's general ophthalmology* (16th ed. New York: McGraw-Hill Medical.

Saccuzzo, D. P., & Braff, D. L. (1981). Early information processing deficit in schizophrenia: New findings using schizophrenic subgroups and manic control subjects. *Archives of General Psychiatry, 38*, 175–179.

Schechter, I., Butler, P. D., Silipo, G., Zemon, V., & Javitt, D. C. (2003). Masking dysfunction in schizophrenia. *Schizophrenia Research, 64*, 91–101.

Schechter, I., Butler, P. D., Zemon, V., Revheim, N., Saperstein, A. M., Jalbrzikowski, M., et al. (2005). Impairments in generation of early-stage transient visual evoked potentials to magno- and parvocellular selective stimuli in schizophrenia. *Clinical Neurophysiology, 116*, 2204–2215.

Schwartz, B. D., McGinn, T., & Winstead, D. K. (1987). Disordered spatiotemporal processing in schizophrenics. *Biological Psychiatry, 22*, 688–698.

Selemon, L. D., & Begovic, A. (2007). Stereologic analysis of the lateral geniculate nucleus of the thalamus in normal and schizophrenic subjects. *Psychiatry Research, 151*, 1–10.

Skottun, B. C., & Skoyles, J. R. (2007a). Contrast sensitivity and magnocellular functioning in schizophrenia. *Vision Research, 47*, 2923–2933.

Skottun, B. C., & Skoyles, J. R. (2007b). Reply to Keri, S. The magnocellular system and schizophrenia. *Vision Research, 48*, 1183–1185.

Slaghuis, W. L. (1998). Contrast sensitivity for stationary and drifting spatial frequency gratings in positive- and negative-symptom schizophrenia. *Journal of Abnormal Psychology, 107*, 49–62.

Slaghuis, W. L. (2004). Spatio-temporal luminance contrast sensitivity and visual backward masking in schizophrenia. *Experimental Brain Research, 156*, 196–211.

Slaghuis, W. L., & Bishop, A. M. (2001). Luminance flicker sensitivity in positive- and negative-symptom schizophrenia. *Experimental Brain Research, 138*, 88–99.

Slaghuis, W. L., & Thompson, A. K. (2003). The effect of peripheral visual motion on focal contrast sensitivity in positive- and negative-symptom schizophrenia. *Neuropsychologia, 41*, 968–980.

Zeppieri, M., & Johnson, C. A. (2008). Frequency doubling technology (FDT) perimetry. *Imaging and Perimetry Society*. mhtml:file://w:Frequency doubling technology(FDT)perimetry.Mht (11.24.09).